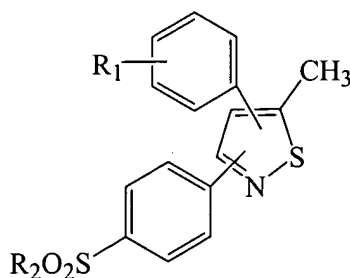


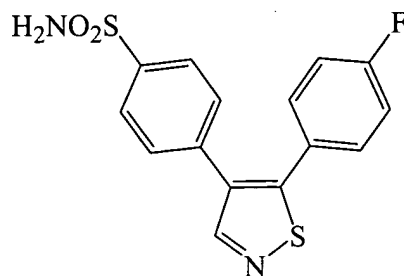
REMARKS

This document is submitted in response to the Office Action of November 16, 2004. Claims 1, 2 and 6 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Ducharme *et al.* U.S. Patent No. 5,840,746 in view of *In re Wood* 199 USPQ 137 (CCPA 1978).

Regarding the rejection the Examiner provides that Applicant claims compounds of the following formula:

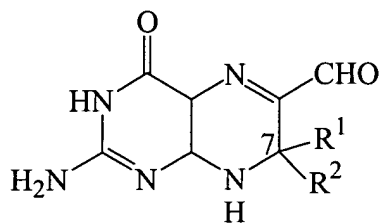


wherein said compounds have antipyretic, analgesic and antiphlogistic activity. With respect to the prior art cited, the Examiner reasons that Ducharme *et al.* teach an isothiazole compound and a pharmaceutical composition with antipyretic, analgesic and antiphlogistic activity. The Examiner maintains that Ducharme *et al.* generically teach the instant claims when their compound has the following structure:

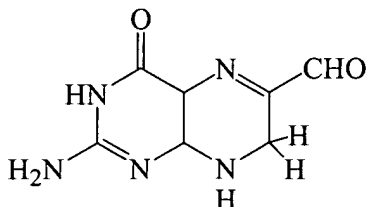


The Examiner reasons that the only difference between this compound and the instant claims is that in the instant claims, the isothiazole is substituted with a methyl. Citing *In re Wood* for the proposition that hydrogen and lower alkyls are obvious variants, the Examiner concludes that one of ordinary skill in the art would be motivated to use the teaching of Ducharme *et al.* to prepare the instant isothiazole compound wherein the hydrogen is substituted for a methyl group.

In re Wood 199 USPQ 137 (CCPA 1978) involved biologically active derivatives of pteridine. The appealed claim was drawn to compounds of the formula:



In one embodiment of the invention R^1 and R^2 were defined as being independently selected from a lower alkyl. In specific embodiments R^1 and R^2 were either dimethyl or diethyl. These compounds were rejected as being obvious over a compound having the following structure:



In affirming the decision of the Board, the court concluded that in view of the close structural similarity of the compounds and the similar antimicrobial activity "one skilled in the art would have been *prima facie* motivated to make the claimed compounds." (*In re Wood* 199 USPQ at 139).

The Examiner bears the burden of establishing a *prima facie* case of obviousness. In determining obviousness, one must focus on Applicant's invention as a whole. Symbol Technologies Inc. v. Opticon Inc., 19 USPQ2d 1241, 1246 (Fed. Cir. 1991). The primary inquiry is:

whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success. . . . Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure.

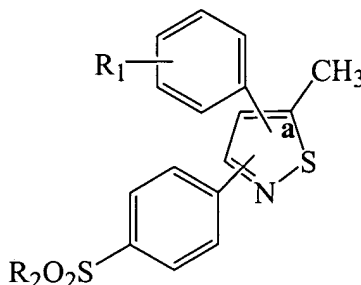
In re Dow Chemical, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). A *prima facie* case of obviousness based on structure exists if the prior art suggests to one of ordinary skill in the art to make the

substitution or modification. In re Taborsky, 183 USPQ 50, 55 (CCPA 1974). If the invention is structurally similar to the prior art, however, nonobviousness can exist if the prior art does not disclose or render obvious a method for making the claimed compound. In re Payne, 203 USPQ 245 (CCPA 1979).

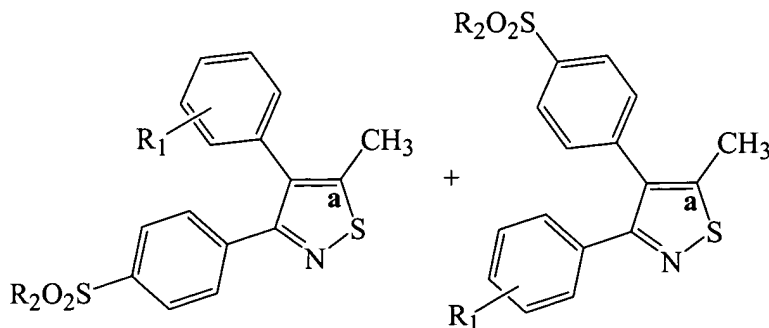
References relied upon to support a rejection under 35 USC § 103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public. . . . An invention is not "possessed" absent some known or obvious way to make it. . . . Hence, the presumption of obviousness based on close structural similarity is overcome where the prior art does not disclose or render obvious a method for making the claimed compound.

In re Payne, 203 USPQ at 255 (citations omitted).

Applicant asserts that the cited references, either alone or combined, do not disclose or suggest the present invention and therefore, do not render the present invention obvious. The present invention describes the synthesis of isothiazole derivatives having the following formula:

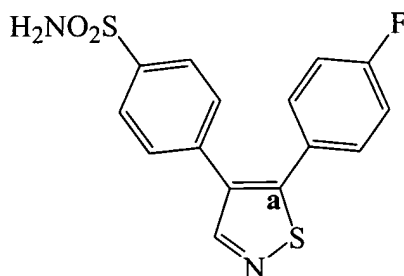


wherein R₁ is hydrogen, hydroxyl or halogen and R₂ is methyl or amino. Included in the present invention is a method for preparing these compounds. Thus the present invention discloses trisubstituted isothiazole derivatives having two phenyl groups and a methyl group on the carbon atom directly adjacent to the sulfur of the isothiazole ring (a) as illustrated by the following structures:



These compounds have anitpyuretic, analgesic and antiphylogistic activity. Additionally, as illustrated in the Experimental results set forth in Example 9, these compounds also selectively inhibit COX-2 relative to COX-1. (Specification, pages 41 - 43). As explained in the Specification, this property minimizes the side effects associated with conventional COX-2 inhibitors. (Specification, page 14, line 27 - page 15, line 17).

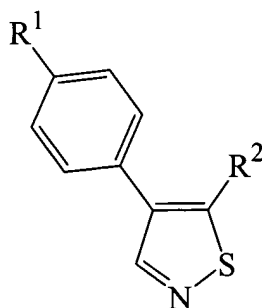
As noted by the Examiner in one embodiment Ducharme *et al.* disclose a compound having the following formula:



The Examiner maintains that the difference between this compound and the compounds of the instant invention is the substitution of a hydrogen atom for a methyl group. Citing *In re Wood*, the Examiner concludes that one of ordinary skill in the art would be motivated to use the teaching of Ducharme *et al.* to prepare the instant isothiazole compound wherein the hydrogen is substituted for a methyl group. Applicant respectfully disagrees with this assertion and maintains that this compound has a completely different structure from the compounds of the instant invention. As noted above, the compounds taught by the instant method are trisubstituted isothiazole derivatives having two phenyl groups and a methyl group directly adjacent to the sulfur of the isothiazole ring (a). Contrary to the Examiner's assertion the compound illustrated

above does not substitute a hydrogen for a methyl group at the carbon adjacent to the sulfur (a), but rather in the compound illustrated above a phenyl group is positioned at the carbon directly adjacent to sulfur atom (a). Applicant maintains that these compounds have different structural formulas and consequently different chemical properties and activities. Because of this Applicant maintains that one of ordinary skill in the art would not be motivated to use the teaching of Ducharme *et al.* to prepare the instant isothiazole compounds.

Assuming for the sake of argument that a *prima facie* case of obviousness has been made by the Examiner, Applicant contends that Ducharme *et al.* do not teach or suggest a method for preparing the trisubstituted isothiazole derivatives of the instant invention. Ducharme *et al.* teach a method for preparing disubstituted isothiazole derivatives having the following structure:



(Specification, col. 3, lines 41-65, col. 37, lines 35-55). Ducharme *et al.* do not teach or suggest a method for preparing trisubstituted isothiazole derivatives. As outlined above, the law is clear that the presumption of obviousness based on close structural similarity is overcome where the prior art does not disclose or render obvious a method for making the claimed compound. Applicant therefore respectfully requests that this rejection be withdrawn.

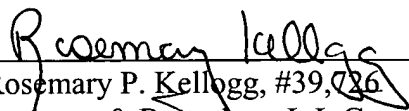
Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Appl. No. 10/681,919
Amdt. dated February 16, 2005
Reply to Office Action of November 16, 2004

Respectfully submitted,

Date February 16, 2005


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